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PRINCIPAL INVESTIGATOR: Rick Williams

CONTRACTING ORGANIZATION: RESEARCH TRIANGLE INSTITUTE
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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The goal of the PASA Consortium is to fund research that aims to identify and develop new medications to improve treatment outcomes for alcohol and substance use disorders (ASUD), especially those that occur concurrently with traumatic brain injury (TBI) and post-traumatic stress disorder (PTSD). In the second year, the consortium launched 3 studies with corresponding subcontracts, and pursued 2 additional studies and subcontracts. In tandem with the start-up of the new studies, the consortium solicited new studies through the second RFA processes, and selected a study to receive funding for a planning grant.

15. SUBJECT TERMS

None listed

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1. Introduction

The goal of the PASA Consortium is to fund research that aims to identify and develop new medications to improve treatment outcomes for alcohol and substance use disorders (ASUD), especially those that occur concurrently with traumatic brain injury (TBI) and post-traumatic stress disorder (PTSD). Clinical trials that include military service member and Veteran populations are highly desirable because this comorbidity, along with mild to moderate TBI, is common in these populations. Alcohol use disorder (AUD) is the most common ASUD in the military, but opiate use disorder (OUD) also has developed significant clinical importance due to prolonged pain treatments with opiates. FDA approved pharmacotherapies are available for ASUD, OUD, and PTSD. While TBI is of interest, it has no FDA approved specific pharmacotherapies, and none of these combined disorders have FDA approved pharmacotherapies. Under a Cooperative Agreement, RTI International is partnering with the CDMRP to solicit, select, and operationalize research studies that support the goals of the PASA Consortium.

The PASA Consortium has three aims under the primary objective to develop medications to treat ASUD in the context of the reciprocal relationship between ASUD, the physiological state of stress, and the subjective state of anxiety as manifested in PTSD or TBI. The three broad aims are:

AIM 1. Discover novel medications and combination medications for ASUD
AIM 2. Develop these medications through a rational Phase I proof of concept pipeline
AIM 3. Conduct Phase II preliminary safety and efficacy trials of potential medication combinations in optimal target populations and explore functional genetic polymorphisms for matching patients to these medications

2. Keywords

alcohol and substance use disorders
post-traumatic stress disorder
traumatic brain injury
request for applications
pharmacotherapy
research consortium

3. Accomplishments

Our primary objectives for the second year were:

- To finalize the research protocols for the four studies selected by the GSC in Year 1.
- To open all four studies and begin patient recruitment and animal testing according to schedule.
- To monitor study progress and site performance and adjust protocols, budgets, and contracts as needed.
- To issue another request for applications for a large Phase II human study and conduct all subsequent related activities including proposal review, proposal selection, and subsequent protocol development and study launch.

- Begin exploring data analysis and publication opportunities according to the consortium publication policy.

3.1 Discovery Studies

3.1.1 "Assessing pharmacotherapies in animal models of post-traumatic stress disorder and alcohol use disorder" (Principal Investigators: Drs. Colin N. Haile, Therese A. Kosten)

PTSD and AUD are linked to dysregulated noradrenergic (NE) function, altered hypothalamic-pituitary-adrenal (HPA) axis stress reactivity, and the endogenous opioid dynorphin and its receptor (kappa opioid receptor, KOR) play a significant role in stress reactivity and alcohol reinforcement. Thus, the primary objective of this study is to test the ability of FDA investigational medications that target these systems on their ability to reduce PTSD-induced alcohol intake in a rodent model of PTSD/AUD comorbidity. Original study drugs include CERC-501, candesartan and perindopril. However, study drugs were recently modified to include ASP8062, a drug compound from pharmaceutical company, Astellas, as well as doxazosin and baclofen. These changes to study drugs have been modified accordingly in the study protocol and are currently under ACURO review/approval.

The study has three aims to support this objective:

Aim 1 will evaluate whether medications (i.e. CERC-501, doxazosin, ASP8062) will alter PTSD-like symptoms in a rodent model of PTSD. The hypothesis is that all the drugs will decrease PTSD symptoms.

Aim 2 will evaluate whether medications (i.e., ASP8062 or baclofen) will alter alcohol self-administration. The hypothesis is that the drugs will reduce drinking.

Aim 3 will determine whether medications will alter PTSD-induced increases on alcohol self-administration. This aim is dependent on whether efficacy of ASP8062 is observed in at least one (and ideally both) Experiments 1 and 2. This experiment will include the most efficacious dose of ASP8062 alone (found in AIM 1) and the most efficacious dose of Doxazosin alone (found in AIM 1) and a vehicle control resulting in a total of 3 drug groups.

This study was selected for its alignment with the PASA Discovery aim to develop effective drug therapies for comorbid PTSD/AUD. The strengths of the study include (1) the proposed PTSD model in that, like humans exposed to traumatic stress, only a subset of rats that are exposed demonstrate enduring PTSD-like symptoms, representing a vulnerable population and (2) behaviors other than amount of alcohol consumed will be examined, such as anxiety-like behavior, sensitivity to pain and avoidance of an aversive stimulus all of which mirror human symptoms of PTSD.

1. University of Houston animal protocol amendment approved adding study medications 8/2/2016
2. Interim funding obtained from University of Houston, Department of Psychology 9/1/2016
3. Animal protocol approved by ACURO 12/20/2016
4. Graduate student recruited and trained 1/2/2017

5. Animal Study Manual of Operations drafted 1/27/2017
6. Experiments planned, coordinated and initiated 3/13/2017
7. University of Houston animal protocol 3-year renewal approved 6/2/2017
8. PI formally notified by University of Houston of sub-award funding 6/9/2017
9. Amendment to add new test articles approved 8/15/2017

Behavioral Testing

At present, all experiments have been halted due to protocol review by ACURO and changes in test medications. These and other issues that have delayed progress are elaborated on below. Thus, these ongoing experiments have low numbers of animals in each group preventing statistical analysis and limiting data interpretation.

AIM 1: Evaluate whether medications (e.g. CERC-501, doxazosin, ASP8062,) will alter PTSD-like symptoms in a rodent model of PTSD.

General protocol description: To fulfill the objectives of AIM 1 of our proposal, we use the predator odor exposure stress model. In rodents, exposure to predator odor is associated with PTSD-like behaviors including increased anxiety and avoidance behavior. These behaviors are typically measured with elevated plus maze (EPM), open field test (OFT) and contextual avoidance conditioning procedures or conditioned place aversion (CPA). In general, predator odor exposure decreases time spent on the open arms and increases time spent in the closed arms of the EPM. Predator odor exposure also decreases time spent in the center of the open field in the OFT. Finally, in the CPA tests predator odor exposure decreases time spent in the predator odor-paired context in the avoidance test. Results from these behavioral tests assessing CERC-501 is presented below.

Testing protocol: Adult male Sprague-Dawley rats (Charles River Labs; Wilmington, MA, N=34) were used in the studies. Baseline measures were obtained first in all behavioral assays before predator odor exposure. Rats were then exposed to predator odor and tested again in all behavioral paradigms. On Day 6, rats were then administered various doses of CERC-501 (0, 1, 3, and 10mg/kg, PO) for 5 days and their behavior again assessed in the behavioral assays on Days 9-10. The timing of the testing schedule was based on our preliminary data and previous studies. Individuals performing the behavioral tests were blind to the dose of medication administered. The testing procedure for each behavioral assay is detailed below.

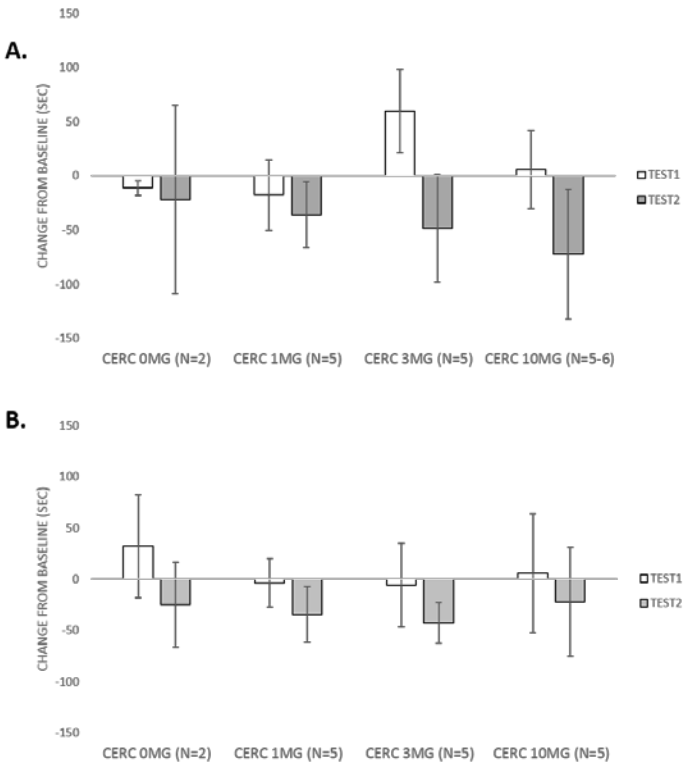
Avoidance contextual conditioning: The conditioning apparatus (MED Associates, St. Albans, VT) consists of two primary chambers that differ by floor texture (tactile, rods vs mesh), color (visual, white vs black) and lighting separated by a central compartment designed to provide a neutral starting position. Automatic Guillotine doors on either side of the center compartment allow doors to be opened simultaneously to both primary chambers without interference. Animal position is tracked by IR photobeam detectors. The central compartment and two primary chambers include a stainless-steel waste pan located directly beneath the floor. Rats were first exposed to the conditioning apparatus (MED Associates) for 15 min with full access to obtain baseline times spent in each chamber (baseline). The next day rats were randomly assigned to a compartment and exposed to no odor for 15 min in the morning (AM session), then returned to their homecage.

In the evening of the same day (PM session) rats were confined to the opposite compartment and exposed to bobcat urine (15 min) soaked filter paper in a disposable weigh-boat placed under the floor of the apparatus in the waste pan. The following day (Avoidance Test), rats were again allowed to explore the entire apparatus (15 min) and times spent in each chamber obtained. Avoidance of predator-paired context was quantified as post-conditioning time in predator context minus pre-conditioning time in predator context (change from baseline, seconds).

Results: Figure 1 presents preliminary data on the impact of various doses of CERC-501 in rats exposed to predator odor stress (A) and no predator odor stress (B). "TEST1" was performed 24 hours after odor/no odor exposure whereas "TEST2" was performed 10 days after odor/no odor exposure. As noted, the low numbers per group and wide variability prevent any statistical analysis or interpretation.

Elevated Plus Maze: We utilized the elevated plus maze (EPM) test to examine the effects of predator odor exposure on anxiety-like behavior as we have previously published. The EPM consists of two open arms (45-cm long × 10-cm wide), two closed arms (45-cm long × 10-cm wide × 30-cm high), and a middle compartment (4-cm long × 4-cm wide) forming the shape of a plus. The EPM is elevated 50-cm above the ground. The floor of the EPM and the walls of the enclosed are made of black acrylic. Rats were first habituated to the testing room for 30-min before testing with no experimenter present in the room. During testing each rat is placed in the middle compartment (head facing an open arm) and allowed to freely explore the apparatus for 5-min. The apparatus is cleaned with disinfectant after each 5-min run. The movements of each rat are recorded by a digital video camera mounted at a height of 130-cm and connected to a computer. Testing is conducted under red-light. For the present study, data were analyzed by an automated software program (EthoVision XT, Version 12.0, Wageningen, The Netherlands). Percent time spent in the open and closed arms of the EPM and as well as time spent in the center zone were calculated.

Figure 1. Impact of CERC-501 on conditioned place aversion in rats exposed and not exposed to predator odor stress.



Results: Preliminary data on the impact of various doses of CERC-501 on EPM measures in rats exposed to predator odor stress and no predator odor stress are presented in Figure 2 and Figure 3 respectively. Data are presented for baseline (A), 24 hours post-odor/no odor exposure (B) and following 5 days of CERC-501administration on day 10 (C) in both figures. Primary measures include % time spent in the center, open and closed arms of the EMP apparatus. As shown in Figure 2, the low numbers per group and wide variability prevent any statistical analysis or interpretation. Although pure speculation, as seen in Figure 2 C, CERC-501 appears to be associated with a dose-dependent increase in time spent in the closed arm which would suggest an increase in predator odor stress effects. Figure 3 shows data presented for baseline (A), 24 hours no-odor exposure (B) and following 5 days of CERC-501administration on day 10 (C). No apparent effects of CERC-501 on any EPM measure were observed.

Figure 2. Impact of CERC-501 on elevated plus maze measures in rats exposed to predator odor stress.

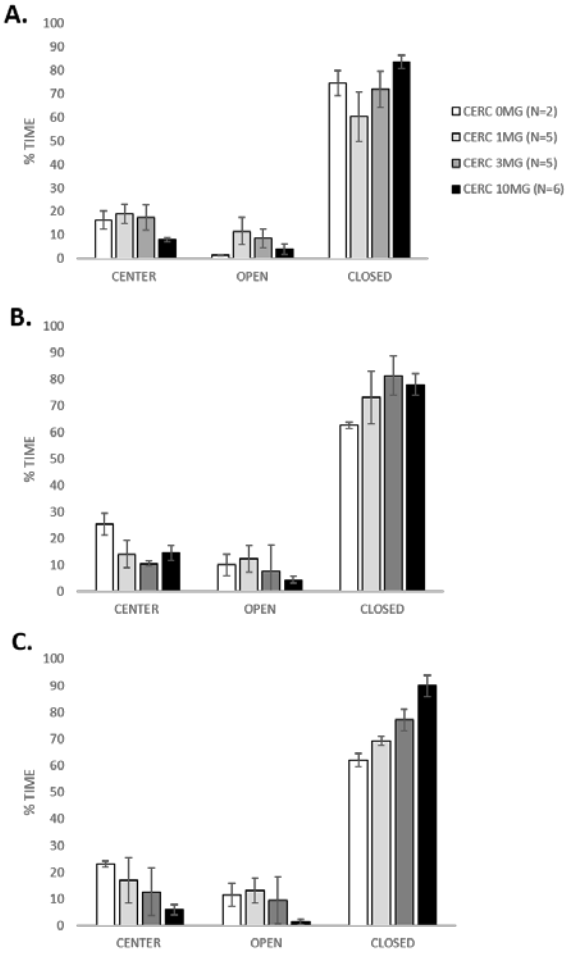
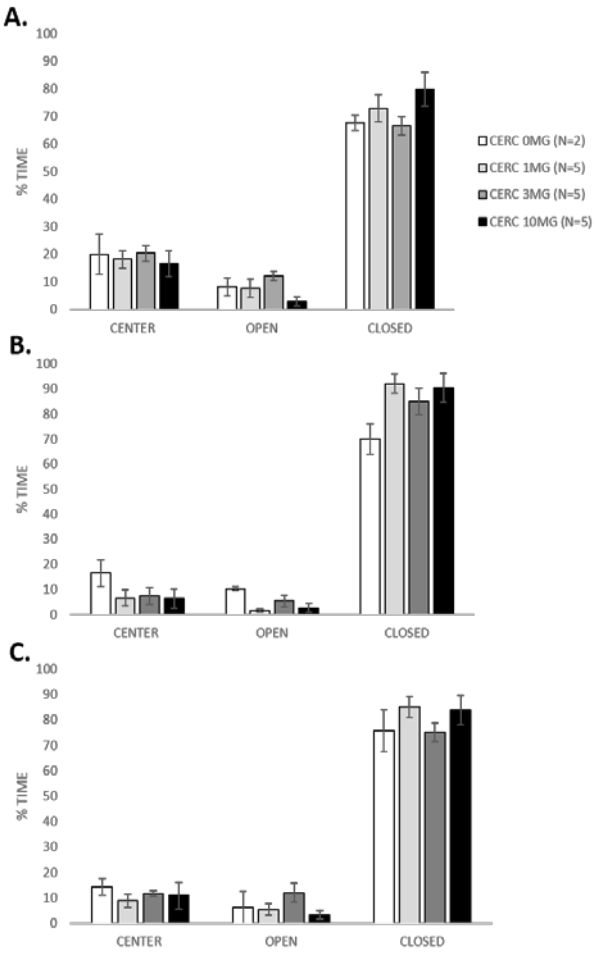


Figure 3. Impact of CERC-501 on elevated plus maze measures in rats not exposed to predator odor stress.



Open field: We used the open field test as an additional measurement of anxiety-like behavior. Our open field apparatus are constructed of a Plexiglas arena (17 " L x 17" W x 12" H (43.2 cm x 43.2 cm x 30.5 cm; MED Associates, Fairfax, VT) with infra-red emitter and detectors around the perimeter that detect different measures of activity. The test is initiated by placing the animal in the center of the open field

chamber and behavior recorded for 30 minutes. The observer is not present in the room during testing. Testing is conducted under red-light. Boxes are cleaned thoroughly between subjects. Data are collated as time spent in the center of the open field according to the manufacturers pre-set defined parameters for center area.

Results: Preliminary data on the impact of various doses of CERC-501 on open field measures in rats exposed to predator odor stress and no predator odor stress are presented in Figure 4 and Figure 5 respectively. Data are presented for baseline (A), 24 hours post-odor/no odor exposure (B) and following 5 days of CERC-501administration on day 10 (C) in both figures. As noted, the number of animals in each group precludes any statistical analysis. Although speculative, Figure 4 C appears to suggest CERC-501 10mg decreased zone entries and zone time compared to their respective baselines. A decrease in zone entries and zone time is consistent with enhancement of predator odor-induced stress effects.

Figure 4. Impact of CERC-501 on open field test measures in rats exposed to predator odor stress.

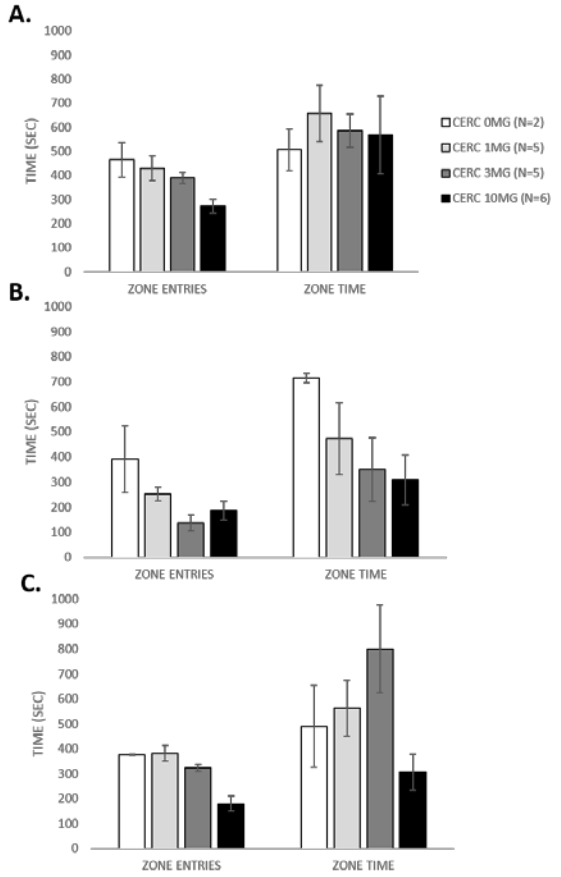
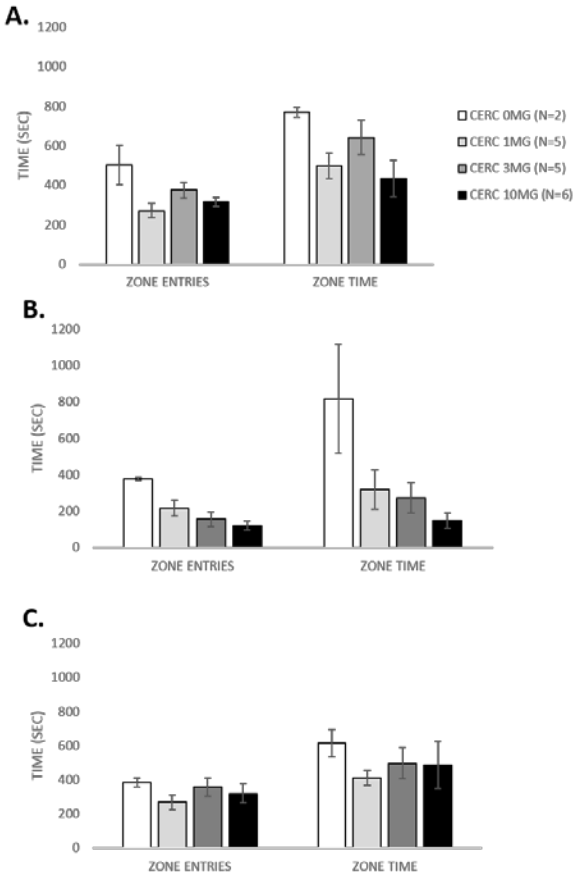


Figure 5. Impact of CERC-501 on elevated plus maze measures in rats not exposed to predator odor stress.



Future Plans

1) Add doxazosin as a test article in AIM1 and AIM3. We have shown in a small human clinical trial that doxazosin significantly decreased PTSD symptomology. Doxazosin will serve as a positive control.

2) Add ASP8062 as a test article in all AIMs. ASP8062 is a GABA B receptor positive allosteric modulator (PAM) presently in phase 3 clinical trials for the treatment of fibromyalgia. GABA B PAMs have been shown to decrease alcohol self-administration in rodents. ASP8062 will be assessed in AIMs 1 and 2.

3) Add baclofen as a test article. Baclofen will serve as a positive control for AIM2 in the alcohol self-administration study.

Changes in test drugs have been approved by the University of Houston IACUC (UH IACUC). Changes are presently under review by ACURO. Experiments are presently on hold pending review outcome.

Current Problems/Issues

1) ACURO's review of the already approved animal protocol by UH IACUC significantly delayed initiation of experiments.

2) ACURO is presently reviewing suggested changes in test articles. The same questions were raised as under the previous review regarding the protocol that ACURO had previously approved. Experiments have been halted and this process continues to delay our studies.

3) Documents requested by ACURO that they should already have were blocked by their email system. Therefore we are unable to forward requested documents. This was not the case previously. ACURO has acknowledged this as an issue that is being addressed.

4) Test articles have been changed multiple times due to numerous factors.

5) An overly complex randomizing of drug administration scheme resulted in miss-dosing of animals. A more realistic randomization scheme has since been employed to resolve this issue.

6) The agreement between the pharmaceutical company that owns ASP8062 (Astellas) and University of Houston has been under legal review and continues to delay us including this compound to test.

3.1.2 **"Preclinical Analysis of Combined Zonisamide and Doxazosin Treatments in Stress---Alcohol Drinking Models"** (Principal Investigator: Dr. Howard C. Becker)

The primary objective of this study is to test the efficacy of zonisamide and doxazosin (independently or in combination) on a) stress-induced alcohol drinking and b) PTSD-induced alcohol drinking. The study has two aims to support this objective:

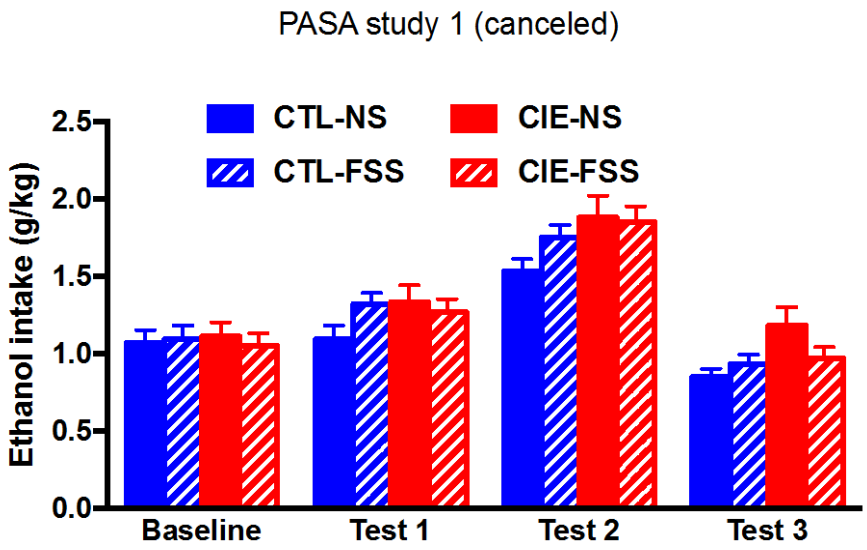
Aim 1: Examine effects of zonisamide and doxazosin treatments, alone or in combination, on stress-facilitation of drinking in alcohol dependent vs. non-dependent male and female mice.

Aim 2: Determine effects of zonisamide and doxazosin treatments, alone or in combination, on drinking in a PTSD-alcohol dependence model in male and female mice.

The study design initially included use of the drug compound carisbamate. Due to issues surrounding drug availability, it was decided that zonisamide be used in place of carisbamate, and the study protocol was modified to reflect this change in March of 2017, and the change was

approved by ACURO on April 25, 2017. Additional study updates are as follows:

1. 128 male mice were ordered from JAX labs. 27-APR-2017
2. Mice started the baseline period of voluntary alcohol intake. 4-MAY-2017
3. Results for Test Cycle 1 were shared via email. Results failed to show an increase in ethanol intake in mice that experienced CIE exposure and stress. 5-JUL-2017
4. Instructions for the preparation of Zonisamide were discussed. 12-JUL-2017
5. Results for Test Cycles 1-3 (shown in chart below) were shared via email and discussed in a conference call. The main issue was that the expected phenotype was not observed. Specifically, mice treated with CIE exposure and stress did not exhibit the expected increase in ethanol intake, thereby obviating evaluation of the ability of drug treatments to reduce such an effect. This was due to ongoing construction occurring in the research facility where mice were being housed. Consequently, a decision was made to abort the study and start with a new group of mice. 16-AUG-2017
6. Mice from this aborted study were used to test doses of Doxazosin and Zonisamide that we plan to use in the experiment. 17-AUG-2017
7. The MUSC protocol was amended to indicate an increase in the number of mice that will be used in this project. This amendment was then approved by MUSC IACUC. 28-AUG-2017
8. The approved IACUC amendment and associated documentation related to increasing the animal sample size were then sent on to ACURO for approval, which was obtained 15-SEP-2017
9. A new set of mice (n= 128) was ordered to restart Aim 1. 16-SEP-2017
10. Mice began baseline ethanol intake. 23-SEP-2017



Reportable Outcomes

1. The experiment was progressing as expected. Evaluation of baseline ethanol intake was completed, mice were separated in the different experimental groups using a randomization protocol provided by Benjamin Carper. 23-JUN-2017

2. The experiment addressing Aim 1 failed to show the expected phenotypic (behavioral) result. After some discussion, a decision was made to cancel this study and to start with a new group of mice. Also, the mice from the failed study were used to pilot the doses of Doxazosin and Zonisamide that will be used in the next study. 16-AUG-2017

Future Plans

The data obtained in this new study will be analyzed to decide when treatment with Doxazosin and Zonisamide can start.

3.2 Proof of Concept Studies

3.2.1 "Efficacy and Safety Study of PT150 (formerly ORG 34517) in Veterans with Co-morbid PTSD/AUD" (Principal Investigator: Dewleen G. Baker, MD)

The primary objective of this study is to test the efficacy, safety, and tolerability of a novel GR antagonist PT150 (formerly ORG 34517) for AUD/PTSD dual diagnosis treatment in veterans. The study has two aims to support this objective:

Aim 1 is to evaluate PT150 treatment compared to placebo taken over 14-days of active treatment, followed by 14 treatment-free days in veterans with co-occurring AUD/PTSD. The hypotheses are (a) extinction recall at 14 days after initiation of treatment will improve, (b) subjectively rated PTSD symptoms, alcohol craving and alcohol consumption at 28 days after initiation of treatment will be reduced; and (c) the treatment will be safe and well tolerated.

Aim 2 is to evaluate the safety of study drug PT150 taken concurrently with alcohol consumption, in 10 non-treatment seeking AUD subjects by evaluating safety endpoints (vital signs, laboratory measures, AEs) during alcohol challenge prior to, and after 4 days of PT150 treatment, when PT150 has reached steady state. The hypothesis is that the drug will be safe and well tolerated.

The study aligns with PASA aims for a proof of concept study to assess safety and surrogate markers (extinction learning) of clinical efficacy in PTSD for treatment with an existing drug compound in veterans with AUD combined with PTSD. The medication is novel and innovative, and the mechanism of action (GR antagonism) for treatment of the key symptoms/behaviors is supported by previous research, including two clinical trials currently underway (PTSD in veterans, AUD is non-veterans) using a drug with a similar mechanism of action. The efficacy is likely via modulation of the stress-axis, which is a logical target for the PTSD+AUD population.

The study team and the PASA leadership jointly decided to remove Aim 2 as a component of this study and consider it as a separate study. The Aim 2 study, named "PT150 (Formerly ORG34517) as a Potential Treatment for Alcohol Use Disorder -Alcohol Interaction Study", will be conducted jointly between Dr. Baker and Dr. Verrico at the Baylor College of Medicine and will be completed before Dr. Verrico's study or the Aim 1 portion of Dr. Baker's study are initiated.

Additionally, the FDA suggested during its review of the IND application that a separate pharmacokinetic (PK) study also be conducted prior to carrying out Aim 1 of the originally

proposed study. The study team and PASA leadership are currently working through the study design considerations for the future PK study.

The study protocol is finalized and has been for some time. After briefly being put on clinical hold by the FDA (February 21, 2017) various study-related items were addressed and submitted in response to FDA, at which point the clinical hold was lifted (May 16, 2017). The study team also worked diligently to address non-clinical hold-related items to be as thorough as possible, communicating with FDA between May and July 2017, to success. A Certificate of Confidentiality was also successfully obtained for the study. Study drug has also been received on site by the study team from PopTest, Oncology, the IND holder/pharmaceutical collaborator. The study has not yet launched in the field due to numerous regulatory delays experienced at the site-IRB level. The study requires dual IRB approval from both the Baylor College of Medicine (BCM) IRB as well as the Veterans Affairs Research and Development Committee (the VA's version of the IRB) at the Michael E. DeBakey Veterans Affairs Medical Center. The process was also complicated due to the original PI, Dr. Thomas Newton, departing BCM in Summer of 2017. Now the study team and PASA leadership are anticipating final approval at both the BCM IRB and VA R&D level to occur in November 2017. Presubmission procedures for HRPO are also underway to ensure HRPO submission and approval can occur readily following IRB approval. Study launch will be on track to commence shortly thereafter given that forms development, MOP development, acquisition and licensure for various planned assessment tools, etc. are all on track.

3.2.2 **"Zonisamide as a New Treatment for PTSD & Co-Occurring AUD"** (Principal Investigators**:** Drs. Christopher Verrico and Thomas Kosten)

This study initially set out to determine the safety and potential efficacy of carisbamate for treating PTSD and AUD symptoms in Veterans with PTSD and co-occurring AUD. However, due to issues pertaining to drug availability, the study drug was changed from carisbamate to zonisamide (in early 2017). Additionally, one of the study PI's (Dr. Thomas Newton) departed Baylor during the Summer of 2017, and was replaced by Dr. Thomas Kosten.

The study aligns with PASA aims for a proof of concept study to assess safety and surrogate markers of clinical efficacy in PTSD for treatment with an existing drug compound in veterans with AUD combined with PTSD. It is a short term clinical with outcomes including PTSD severity and alcohol use. There is ample safety data for zonisamide including its interactions with alcohol, and it has a similar therapeutic profile to FDA-approved Topiramate, but with a superior safety profile and longer half-life. The outcome measures are well justified and well validated (if not gold standard) with the populations (PTSD, AUD), and the inclusion of many PhenX toolkit measures is a methodological strength.

Supporting the feasibility of the study are the investigator's established relationship with the study drug manufacturer, the existence of an IND plan, and the density of the veteran population in the greater Houston area and the study teams' existing roles within Houston VA system. Furthermore, recruitment plans are clearly detailed and the research team has an established recruitment record in conducting studies of this type with veterans.

Not having the risk of uncovering AE's during Phase I interaction experiments gives it an advantage for moving forward go larger trials and eventual deployment (further down the pipeline). If successful, this study would provide valuable safety and efficacy data for planning future studies of zonisamide for treatment of AUD and PTSD.

In 2017, the study protocol moved toward finalization and underwent early reviews by the BCM IRB which resulted in subsequent minor modifications. At present time, the IND application has been submitted to FDA (October 2017) and the study team is awaiting word back from FDA. Once an IND number has been assigned and any FDA comments have been addressed, the study protocol will continue to move through site regulatory requirements at the BCM IRB and VA R&D to obtain proper approvals. The Certificate of Confidentiality application has been prepared and is ready for submission once the IND number is assigned by FDA. Study-related components such as forms development, MOP development, acquisition and licensure for various planned assessment tools, etc. are all on track.

3.3 Administrative Deliverables

We executed the subcontracts for all subawards. We submitted all quarterly reports and continued to hold weekly meetings with PASA leadership and with CDMRP and distribute meeting minutes.

3.4 RFP Release and Review

The PASA Study Research Planning Program finalized the pre-application of RFA 2 in September 2016 and sent it to the GSC for approval in November 2016. The completed milestones for the second RFA are as follows:

1. RFA #2 Sent to GSC for Approval 14-Nov-16
2. Issue PASA RFA#2 1-Dec-16
3. Pre-Application Deadline 24-Mar-17
4. Pre-Application Distribution for Peer Review 28-Mar-17
5. Pre-Application Peer Review 18-Apr-17
6. Pre-Application Programmatic Review 9-May-17
7. Invitation to Submit Full Application 1-Jun-17
8. Pre Full Application Submission Teleconferences 8-Jun-17
9. Full Application Deadline 25-Aug-17
10. Application Distribution for Peer Review 8-Sep-17
11. Programmatic Review 15-Sep-17
12. Full Application GSC Review and Meeting 26-Sep-17
13. Notification of Award Recommendation 4-Oct-17

4. Impact

We are unable to assess the major impact of the work conducted to date, as we are still in the initial stages of all research.

5. Changes/Problems

All problems have been described above in the sections 3.1 and 3.2.

6. Products

No products or publications have been developed to date.

7. Participants and Other Collaborating Organizations

a. What individuals have worked on the project?

Name	Project Role	Person Months	Contribution to Project
Williams, Rick L	Principal Investigator	4	No change
Battestilli, Whitney	Clinical Data Manager	4	Maintained consortium website and related infrastructure; Developed CRFs for sponsored studies; Programmed Data Management Systems for sponsored studies; Developed data processing tools for aggregating, normalizing, and cleaning data; Created reports and dashboards to track study progress.
Bradley, Lauren	Public Health Analyst	6	No change
Collins, Doreen	Consortium Clinical Research Manager	2	No change
Dowd, Elita	Financial Analyst	1	Conducted budgeting and forecasting activities for overall project and studies.
Gatto, Gregory	Regulatory Affairs	2	Worked on IND with Pop Test for PT150, attended FDA meetings, provided guidance and support for the IND and clinical activities. Worked on IND for Zonisamide.
Honeycutt, Emily	Statistician	2	Provided statistical support for protocol design, study implementation, data collection, data analysis and FDA submission
Johnson, Madelyn	Administrative Coordinator	1	Scheduled meetings, took minutes.

Kendrick, Amy	SRPP Manager	1	Managed SRPP logistics, RFA distribution and receipt of applications, for pre-application and full application SRPP application processes.
Kennedy, Sara	Coordinator	2	Coordinated human studies, including scheduling calls, taking notes, updating protocols, working on IRB documentation and CoC.
Mendez, Angela	Programmer	2	Created, revised, and annotated CRFs for 3 PASA studies.
Nolen, Tracy	Senior Research Statistician	4	No change
Peeler, Russ	Human Subjects Protectoin leader	2	Managed IRB applications and communications with RTI IRB, and assisted with site IRB applications. Assisted with HRPO applications.
Riggs, Callie	Project Administration Specialist	3	No change
Rogers, Leslie	Regulatory Affairs	1	Worked on IND with Pop Test for PT150, attended FDA meetings, provided guidance and support for the IND and clinical activities. Worked on IND for Zonisamide.
Tang, Yan	Programmer	1	Developed Medidata forms, conducted edit checks, tested systems.
Turner, Eugene	Programmer	5	CRF design, aCRF design, database testing, and created validation specifications for all studies.

Baylor College of Medicine - Management Core		
Kosten, Thomas	BCM Co-Principal Investigator	11
Domingo, Coreen	BCM Site Coordinator	2
Newton, Thomas	BCM Professor Pyschiatry Research	11
Medical University of South Carolina		
Preclinical Analysis of Combined GABA B PAM and Doxazosin Treatments		
Becker, Howard	Principal Investigator	1
Lopez, Marcelo	Co-Principal Investigator	1
Olsen, Anne	Research Technician	1
University of Houston		
Assessing Pharmacotherapies in Animal Models of Post-Traumatic Stress Disorder and Alcohol Use Disorder		
Haile, Colin	Principal Investigator	1
Kosten, Therese	Co-Principal Investigator	1

There have been no contractual changes since the last reporting period.

DoD Alcohol and Substance Abuse Consortium Award

Pharmacotherapies for Alcohol and Substance Abuse (PASA) Consortium

PI: Rick Williams, PhD & Thomas Kosten, MD **Org:** RTI International

Study Research Planning Program RFA #1 – Aims 1 and 2

- Discover novel medications and combination medications for ASUD.
- Develop medications through a Phase I proof of concept pipeline.

Study Research Planning Program RFA #2 – Aim 3

- Conduct Phase II preliminary safety and efficacy trials of potential medication combinations in PTSD & TBI target populations and explore functional genetic polymorphisms for matching patients to medications.

The SRPP RFA process netted 8 applications, of which 3 were invited to submit full applications. One proposal was recommended for planning grant funding based on scientific merit and alignment with consortium programmatic objectives.

Timeline and Cost

Activities	Q1	Q2	Q3	Q4
Launch Animal Studies				
Monitor animal study progress, site performance				
Protocol Planning, FDA, HRPO, IRB approvals for Human Studies				
SRPP RFA 2				
Estimated Cost (k)	$222	$239	$394	$343

YR2 Completed Objectives

- Executed subcontracts for 3 studies
- Monitored study progress
- Assisted Haile study with ACURO changes
- Completed second SRPP RFA

YR2 Objectives in Progress

- Ongoing study procedures/experimentation being carried out for 2 animal studies
- Ongoing subcontracting and study launch process for 2 clinical studies
- Study design for third clinical study (PT150 PK study) underway